CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number : 088634

Trade Name : AMITRIPTYLINE HCL 100MG TABLETS

Generic Name: Amitriptyline HCL 100mg Tablets

Sponsor : Danbury Pharmacal, Inc.

Approval Date: March 2, 1984

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION 088634

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tenative Approval Letter				
Approvable Letter				
Final Printed Labeling	X			
Medical Review(s)				
Chemistry Review(s)	X			
EA/FONSI				
Pharmacology Review(s)				
Statistical Review(s)				
Microbiology Review(s)				
Clinical Pharmacology Biopharmaceutics Review(s)				
Bioequivalence Review(s)				X
Administrative Document(s)	X			
Correspondence				

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 088634

APPROVAL LETTER

NDA 88-634

3/2/84

Danbury Pharmacal, Inc.
Attention: Nessim Maleh
131 West Street, P.O. Box 296
Danbury, CT 06810

Gentlemen:

Reference is made to your abbreviated new drug application dated December 9, 1983, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Amitriptyline Hydrochloride Tablets, 100 mg.

Reference is also made to our letter dated January 27, 1984 and your response dated February 22, 1984 enclosing final printed labeling and additional information.

The application provides for you to repackage the drug product filed by [redacted] (b)4 - Confidential Business [redacted]

We have completed the review of this abbreviated new drug application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved.

Any significant change in the conditions outlined in this abbreviated new drug application requires an approved supplemental application before the change may be made, except for changes made in conformance with other provisions of Section 314.8 of the new drug regulations.

This Administration should be advised of any change in the marketing status of this drug.

For Initial Campaigns: We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your immediate advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Advertising and Labeling (HFN-240). Also, please do not use Form FD-2253 for this submission.

For Subsequent Campaigns: We call your attention to Regulation 21 CFR 310.300 (b)(3) which requires that material for any subsequent advertising or promotional campaigns, at the time of their initial use, be submitted to our Division of Drug Advertising and Labeling (HFN-240) with a completed Form FD-2253. A copy of Form FD-2253 is enclosed for your convenience.

The enclosures summarize the conditions relating to the approval of this application.

Sincerely yours,

Marvin Seife 3/2/84

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs and Biologics

Enclosures:
Conditions of Approval of a New Drug Application
Records & Reports Requirements
Form FD 2253

cc: BOS-DO
HFN-530
HFN-5
HFN-313
HFN-616
KJohnson/JMeyer/CSmith
R/D INITIAL JMeyer
mm:3/1/84 (0798A)
Approved
C Smith 3-1-84
JMeyer 3/1/84

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 088634

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW (If necessary, continue any item on 8½" x 11" paper. Key continuation to item by number.)

ORGANIZATION: HFN 322

ANDA NUMBER: 88-654

3. NAME AND ADDRESS OF APPLICANT (City and State)

Danbury Pharmacal (Repackager)
Danbury, CT 06810

4. AF NUMBER

5. SUPPLEMENT (S)

NUMBER(S)	DATE(S)

6. NAME OF DRUG

Amitriptyline hydrochloride

7. NONPROPRIETARY NAME

8. SUPPLEMENT(S) PROVIDES FOR:

9. AMENDMENTS AND OTHER (Reports, etc.) DATES

10. PHARMACOLOGICAL CATEGORY

antidepressant

11. HOW DISPENSED

☒ RX ☐ OTC

12. RELATED IND/NDA/DMF(S)

86-854 (manufacturer)

13. DOSAGE FORM (S)

Tablet

14. POTENCY (Iso)

100 mg

15. CHEMICAL NAME AND STRUCTURE

16. RECORDS AND REPORTS

CURRENT ☐ YES ☐ NO

REVIEWED ☐ YES ☐ NO

17. COMMENTS

Applicant satifies requirements as a repackager, manufacturer is (b)4 - Confidential Business

18. CONCLUSIONS AND RECOMMENDATIONS

approval

19. REVIEWER

NAME	SIGNATURE	DATE COMPLETED
C M Smith		

DISTRIBUTION ☐ ORIGINAL JACKET ☐ REVIEWER ☐ DIVISION FILE

Enter evaluation or comments for each item. If necessary, continue on 8" x 10½" paper. Key continuation to item by number. Enter "NC" if no change or "NA" if not applicable.

NDA NUMBER 88-634

22. COMPONENTS AND COMPOSITION (6, 7)

See NDA 86-854

26. FACILITIES AND PERSONNEL (8a,b)

Satisfactory

27. SYNTHESIS (8c)

See NDA 86-854

28. RAW MATERIAL CONTROLS (8d,e)

a. NEW DRUG SUBSTANCE

See NDA 86-854

b. OTHER INGREDIENTS

See NDA 86-854

29. OTHER FIRM(S) (8f)

Manufacturer and applicant in compliance, memo dated 1/4/84..L. Hartley

30. MANUFACTURING AND PROCESSING (8g,h,i,k)

See NDA 86-854

31. CONTAINER (8j)

Glass snd HDPE containers, all tested in accord with USP

32. PACKAGING AND LABELING (8l,m)

satisfactory

33. LABORATORY CONTROLS (In-Process and Finished Dosage Form) (8n)

satisfactory

34. STABILITY (8p)

Protocol submitted, applicant will use 2 year expiry

35. CONTROL NUMBERS (8c)

accounted for

36. SAMPLES AND RESULTS (9)

a. VALIDATION

b. MARKET PACKAGE

37. LABELING (4)

satisfactory per K Johnson

38. ESTABLISHMENT INSPECTION

Applicant and manufacturer in compliance

39. RECALLS

12

CHEMIST'S REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Statement Date:

NDA # 88-634

NAME AND ADDRESS OF APPLICANT:

Danbury Pharmacal Inc
Danbury CT 06810

ORIGINAL XXXX
AMENDMENT
SUPPLEMENT
RESUBMISSION
CORRESPONDENCE
REPORT
OTHER

PURPOSE OF AMENDMENT/SUPPLEMENT

DATE(s) of SUBMISSION(s)

12-9-83

PHARMACOLOGICAL CATEGORY	NAME OF DRUG	HOW DISPENSED
antidepressant	Amitriptyline Hydrochloride	Rx XXX OTC ____
DOSAGE FORM: Tablet	POTENCY(IES): 100 mg	RELATED IND/NDA/DMF: 88-621, 88-620, 88-622, 88-633, 88-634, 88-635, 86-857, 86-859, 86-610, 86-860, 86-854, 86-853
STERILIZATION:	SAMPLES:	

LABELING

To be revised...see medical officer's review

BIOLOGIC AVAILABILITY

N. A. applicant is repackager, manufacturer is [redacted] (b)4 - [redacted]

ESTABLISHMENT INSPECTION

Applicant and manufacturer in compliance

COMPONENTS, COMPOSITION, MANUFACTURING, CONTROLS

controls are satisfactory, all USP testing for final product by repackager requested

PACKAGING

Applicant to use glass and HDPE containers identical to manufacturer

STABILITY:

Protocol: same as manufacturer

Exp. Date: applicant requests 4 years, same as manufacturer, no data, denied. applicant requested to lower expiry to 2 years

REMARKS & CONCLUSION:

Revision requested in labeling 2 year expiry recommended
All compendium tests on final dosage form requested XXXXXXXXXX
Desription of container closure system and tests.
XXXXXXXX non-approval CMSmith

CENTER FOR DRUG EVALUATION AND RESEARCH

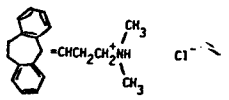
APPLICATION NUMBER 088634

FINAL PRINTED LABELING

AMITRIPTYLINE HYDROCHLORIDE TABLETS, USP

DESCRIPTION: Amitriptyline HCl, a dibenzocycloheptadiene derivative, is a white or practically white, crystalline compound that is freely soluble in water.

It is designated chemically as 10,11-dihydro-N,N-dimethyl-5H-dibenzo [a,d] cycloheptene-Δ^{5},γ -propylamine hydrochloride. The molecular weight is 313.87. The empirical formula is $C_{20}H_{23}N \cdot HCl$, and the structural formula is:



ACTIONS: Amitriptyline HCl is an antidepressant with sedative effects. Its mechanism of action in man is not known. It is not a monoamine oxidase inhibitor and it does not act primarily by stimulation of the central nervous system.

Amitriptyline inhibits the membrane, pump mechanism responsible for uptake of norepinephrine and serotonin in adrenergic and serotonergic neurons. Pharmacologically this action may potentiate or prolong neuronal activity since reuptake of these biogenic amines is important physiologically in terminating its transmitting activity. This interference with reuptake of norepinephrine and/or serotonin is believed by some to underlie the antidepressant activity of amitriptyline.

INDICATIONS: For the relief of symptoms of depression. Endogenous depression is more likely to be alleviated than are other depressive states.

CONTRAINDICATIONS: Amitriptyline HCl is contraindicated in patients who have shown prior hypersensitivity to it. It should not be given concomitantly with monoamine oxidase inhibitors. Hyperpyretic crises, severe convulsions, and deaths have occurred in patients receiving tricyclic antidepressants and monoamine oxidase inhibiting drugs simultaneously. When it is desired to replace a monoamine oxidase inhibitor with amitriptyline, a minimum of 14 days should be allowed to elapse after the former is discontinued. Amitriptyline HCl should then be initiated cautiously with gradual increase in dosage until optimum response is achieved.

This drug is not recommended for use during the acute recovery phase following myocardial infarction.

WARNINGS: Amitriptyline HCl may block the antihypertensive action of guanethidine or similarly acting compounds.

It should be used with caution in patients with a history of seizures and, because of its atropine-like action, in patients with a history of urinary retention, angle-closure glaucoma, or increased intraocular pressure. In patients with angle-closure glaucoma, even average doses may precipitate an attack.

Patients with cardiovascular disorders should be watched closely. Tricyclic antidepressant drugs, including amitriptyline, particularly when given in high doses, have been reported to produce arrhythmias, sinus tachycardia, and prolongation of the conduction time. Myocardial infarction and stroke have been reported with drugs of this class.

Close supervision is required when amitriptyline is given to hyperthyroid patients or those receiving thyroid medication.

This drug may impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle.

Amitriptyline may enhance the response to alcohol and the effects of barbiturates and other CNS depressants. In patients who may use alcohol excessively, it should be borne in mind that the potentiation may increase the danger inherent in any suicide attempt or overdosage. Delerium has been reported with concurrent administration of amitriptyline and disulfiram.

Usage in Pregnancy: Safe use of amitriptyline during pregnancy and lactation has not been established; therefore, in administering the drug to pregnant patients, nursing mothers, or women who may become pregnant, the possible benefits must be weighed against the possible hazards to mother and child.

Animal reproduction studies have been inconclusive and clinical experience has been limited.

Usage in Children: In view of the lack of experience in children, the drug is not recommended at the present time for patients under 12 years of age.

PRECAUTIONS: Schizophrenic patients may develop increased symptoms of psychosis; patients with paranoid symptomatology may have an exaggeration of such symptoms; manic depressive patients may experience a shift to mania or hypomania.

In these circumstances the dose of amitripytline may be reduced or a major tranquilizer such as perphenazine may be administered concurrently.

When this drug is given with anticholinergic agents or sympathomimetic drugs, including epinephrine combined with local anesthetics, close supervision and careful adjustment of dosages are required.

Paralytic ileus may occur in patients taking tricyclic antidepressants in combination with anticholinergic-type drugs.

Caution is advised if patients receive large doses of ethchlorvynol concurrently. Transient delirium has been reported in patients who were treated with one gram of ethchlorvynol and 75-150 mg. of amitriptyline.

The possibility of suicide in depressed patients remains until significant remission occurs. Potentially suicidal patients should not have access to large quantities of this drug. Prescriptions should be written for the smallest amount feasible.

Concurrent administration of amitriptyline and electroshock therapy may increase the hazards associated with such therapy. Such treatment should be limited to patients for whom it is essential.

Discontinue the drug several days before elective surgery if possible.

Both elevation and lowering of blood sugar levels have been reported.

Amitriptyline should be used with caution in patients with impaired liver function.

ADVERSE REACTIONS: Note - Included in the listing which follows are a few adverse reactions which have not been reported with this specific drug. However, pharmacological similarities among the tricyclic antidepressant drugs require that each of the reactions be considered when amitriptyline is administered.

Cardiovascular: Hypotension, hypertension, tachycardia, palpitation, myocardial infarction, arrhythmias, heart block, stroke.

of urinary retention, angle-closure glaucoma, or increased intraocular pressure. In patients with angle-closure glaucoma, even average doses may precipitate an attack.

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Cardiovascular: Hypotension, hypertension, tachycardia, palpitation, myocardial infarction, arrhythmias, heart block, stroke.

CNS and Neuromuscular: Confusional states; disturbed concentration; disorientation; delusions; hallucinations; excitement; anxiety; restlessness; insomnia; nightmares; numbness, tingling, and paresthesias of the extremities; peripheral neuropathy; incoordination; ataxia; tremors; seizures; alteration in EEG patterns; extrapyramidal symptoms; tinnitus; syndrome of inappropriate ADH (antidiuretc hormone) secretion.

Anticholinergic: Dry mouth, blurred vision, disturbance of accommodation increased intraocular pressure, constipation, paralytic ileus, urinary retention, dilation of urinary tract.

Allergic: Skin rash, urticaria, photo-sensitization, edema of face and tongue.

Hematologic: Bone marrow depression including agranulocytosis, leuzopenia, eosinophilia, purpura, thrombocytopenia.

Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, parotid swelling, black tongue. Rarely hepatitis (including altered liver function and jaundice).

Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement and galactorrhea in the female, increased or decreased libido, elevation and lowering of blood sugar levels.

Other: Dizziness, weakness, fatigue, headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, drowsiness.

Withdrawal Symptoms: Abrupt cessation of treatment after prolonged administration may produce nausea, headache, and malaise. Gradual dosage reduction has been reported to produce, within two weeks, transient symptoms including irritability, restlessness, and dream and sleep disturbance. These symptoms are not indicative of addiction. Rare instances have been reported of mania or hypomania occurring within 2-7 days following cessation of chronic therapy with tricyclic antidepressants.

DOSAGE AND ADMINISTRATION: Oral Dosage - Dosage should be initiated at a low level and increased gradually, noting carefully the clinical response and any evidence of intolerance.

Initial Dosage for Adults - Twenty-five mg. three times a day usually is satisfactory for outpatients. If necessary this may be increased to a total of 150 mg. a day. Increases are made preferably in the late afternoon and/or bedtime doses. A sedative effect may be apparent before the antidepressant effect is noted, but an adequate therapeutic effect may take as long as 30 days to develop.

An alternate method of initiating therapy in outpatients is to begin with 50 to 100 mg. amitriptyline HCl at bedtime. This may be increased by 25 to 50 mg. as necessary in the bedtime dose to a total of 150 mg. per day.

Hospitalized patients may require 100 mg. a day initially. This can be increased gradually to 200 mg. a day if necessary. A small number of hospitalized patients may need as much as 300 mg. a day.

Adolescent and Elderly Patients - In general, lower dosages are recommended for these patients. Ten mg. three times a day with 20 mg. at bedtime may be satisfactory in adolescent and elderly patients who do not tolerate higher dosages.

Maintenance: The usual maintenance dosage of amitriptyline HCl is 50 to 100 mg. per day. In some patients 40 mg. per day is sufficient. For maintenance therapy the total daily dosage may be given in a single dose preferably at bedtime. When satisfactory improvement has been reached, dosage should be reduced to the lowest amount that will maintain relief of symptoms. It is appropriate to continue maintenance therapy 3 months or longer to lessen the possibility of relapse.

Usage in Children - In view of the lack of experience in children, this drug is not recommended at the present time for patients under 12 years of age.

Plasma levels: Because of the wide variation in the absorption and distribution of tricyclic antidepressants in body fluids, it is difficult to directly correlate plasma levels and therapeutic effect. However, determination of plasma levels may be useful in identifying patients who appear to have toxic effects and may have excessively high levels, or those in whom lack of absorption or noncompliance is suspected. Adjustments in dosage should be made according to the patient's clinical response and not on the basis of plasma levels.

OVERDOSAGE: Manifestations - High doses may cause temporary confusion, distrubed concentration, or transient visual hallucinations. Overdosage may cause drowsiness; hypothermia; tachycardia and other arrhythmic abnormalities, such as bundle branch block; ECG evidence of impaired conduction; congestive heart failure; dilated pupils; convulsions; severe hypotension; stupor; and coma. Other symptoms may be agitation, hyperactive reflexes, muscle rigidity, vomiting, hyperpyrexia, or any of those listed under ADVERSE REACTIONS.

All patients suspected of having taken an overdosage should be admitted to a hospital as soon as possible. Treatment is symptomatic and supportive. Empty the stomach as quickly as possible by emesis followed by gastric lavage upon arrival at the hospital. Following gastric lavage, activated charcoal may be administered. Twenty to 30 g. of activated charcoal may be given every four to six hours during the first 24 to 48 hours after ingestion. An ECG should be taken and close monitoring of cardiac function instituted if there is any sign of abnormality. Maintain an open airway and adequate fluid intake; regulate body temperature.

The intravenous administration of 1-3 mg. of physostigmine salicylate has been reported to reverse the symptoms of tricyclic antidepressant poisoning. Because physostigmine is rapidly metabolized, the dosage of physostigmine should be repeated as required particularly if life threatening signs such as arrhythmias, convulsions, and deep coma recur or persist after the initial dosage of physostigmine. Because physostigmine itself may be toxic, it is not recommended for routine use.

Standard measures should be used to manage circulatory shock and metabolic acidosis. Cardiac arrhythmias may be treated with neostigmine, pyridostigmine, or propranolol. Should cardiac failure occur, the use of digitalis should be considered. Close monitoring of cardiac function for not less than five days is advisable. Anticonvulsants may be given to control convulsions. Amitriptyline increases the CNS depressant action, but not the anticonvulsant action of barbiturates; therefore, an inhalation anesthetic, diazepam, or paraldehyde is recommended for control of convulsions.

Dialysis is of no value because of low plasma concentrations of the drug.

Since overdosage is often deliberate, patients may attempt suicide by other means during the recovery phase.

Deaths by deliberate or accidental overdosage have occurred with this class of drugs.

HOW SUPPLIED:

Amitriptyline Hydrochloride Tablets are supplied in the following strengths and sizes:

10 mg. tablets, pink, film-coated, round, convex in bottles of 100, 1000, and 5000.

25 mg. tablets, green, film-coated, round, convex in bottles of 100, 1000 and 5000.

50 mg. tablets, brown, film-coated, round, convex in bottles of 100, 1000 and 5000.

75 mg. tablets, purple, film-coated, round, convex in bottles of 100, 1000 and 5000.

100 mg. tablets, orange, film-coated, round, convex in bottles of 100, 1000 and 5000.

150 mg. tablets, green, film-coated, round, convex in bottles of 100, 1000 and 5000.

Plasma levels: Because of the wide variation in the absorption and distribution of tricyclic antidepressants in body fluids, it is difficult to directly correlate plasma levels and therapeutic effect. However, determination of plasma levels may be useful in identifying patients who appear to have toxic effects and may have excessively high levels, or those in whom lack of absorption or noncompliance is suspected. Adjustments in dosage should be made according to the patient's clinical response and not on the basis of plasma levels.

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10 mg. tablets, pink, film-coated, round, convex in bottles of 100, 1000, and 5000.

25 mg. tablets, green, film-coated, round, convex in bottles of 100, 1000 and 5000.

50 mg. tablets, brown, film-coated, round, convex in bottles of 100, 1000 and 5000.

75 mg. tablets, purple, film-coated, round, convex in bottles of 100, 1000 and 5000.

100 mg. tablets, orange, film-coated, round, convex in bottles of 100, 1000 and 5000.

150 mg. tablets, green, film-coated, round, convex in bottles of 100, 1000 and 5000.

Dispense in well-closed, light-resistant containers as defined in the USP.

CAUTION: Federal law prohibits dispensing without prescription.

Manufactured by:
IKAPHARM, LTD
Kfar Saba, Israel
Distributed by:
DANBURY PHARMACAL, INC.
Danbury, Connecticut 06810, USA

Revised: February, 1984
5456, 5457, 5458, 5459, 5558, 5559

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 088634

ADMINISTRATIVE DOCUMENTS

JAN 27 1984

NDA 88-634

Danbury Pharmacal, Inc.
Attention: Nessim Maleh
131 West Street
P.O. Box 296
Danbury, CT 06810

Gentlemen:

Please refer to your abbreviated new drug application dated December 9, 1983 submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for the preparation Amitriptyline Hydrochloride Tablets USP, 100 mg.

The application provides for you to repackage the drug product filed by [redacted] (b)4 - Confidential Business [redacted]

The application is deficient and therefore not approvable under Section 505(b) of the Act as follows:

1. It fails to provide adequate information in the labeling. We recommend the following:

   Revise the package insert in accord with the accompanying labeling guideline.

   In addition, delete the "a" from the Federal Caution statement that appears at the bottom of the insert.

   Also provide for the name and place of business of the manufacturer and/or distributor.

   At the time of the next printing, consider printing the strength of product in bolder print on the container label since it appears on the same line as "USP."

2. It fails to assure that the dosage form has the proper identity, quality, purity and strength. We recommend that you conduct all compendial tests and specifications on the drug product.

3. It fails to include a description and tests that you use for your container/closure system.

4. It fails to include an expiration dating based upon stability data for the drug product when packaged in your container/closure system. In lieu of this data, we recommend that you use a tentative 2 year expiration dating.

5. It fails to include a properly executed Form FDA 356H. (Check the block marked Abbreviated application.)

The file is now closed. If you wish to reopen it, the submission should be in the form of an amendment to this application, adequately organized, which represents the information necessary to remove all deficiencies we have outlined. For those deficiencies related to package insert labeling, we suggest that you incorporate the suggestions noted, then prepare and submit draft copy for our review and comment.

If you do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.110(d). If you do so, the application shall be approved or you shall be given a written notice of opportunity for a hearing on the question of whether the application is approvable.

Sincerely yours,

Marvin Seife 1/27/84

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs and Biologics

Enclosure: Labeling Guidelines

cc: BOS-DO
HFN-530
KJohnson/JMeyer/CSmith
R/D INITIAL JMeyer/MSeife
mm:1/26/84 (4706c)
Not Approvable

C.M. Smith 1-26-84
JMeyer 1/26/84

REVIEW OF PROFESSIONAL LABELING

ANDA - FPL

DATE OF REVIEW: 1-9-84

ANDA #: 88-633 (75 mg)
88-634 (100 mg)
88-635 (150 mg) NAME OF FIRM: Danbury

NAME OF DRUG: Generic: Amitriptyline Hydrochloride Tablets

DATE OF SUBMISSION: 12-9-83

COMMENTS:

Container: Satisfactory (100s, 1000s, 5000s)

However, we encourage the firm to consider placing USP on the line above the strength.

Insert: Not satisfactory

a) Must revise as per our current Guideline

b) CAUTION: Delete "a"

c) Also, must add name and place of business of the manufacturer and/or distributor.

d) The HOW SUPPLIED section must include only those strengths and contaienrs which are approved.

RECOMMENDATIONS:

1. Inform firm of the above comment relating to labels.

2. Send current Labeling Guideline.

3. Request that the firm prepare and submit revised insert labeling.

4. The "How Supplied" section must include only those strengths and containers which are approved.

Kent T. Johnson

cc:
dup
KTJ/cl/1-9-84

DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

TO :Manufacturing Review Branch (HFN-322) DATE: 12-28-83
Division of Drug Quality Compliance

FROM :Division of Generice Drugs
Requester's Name DAVID ROSEN PHONE: 443-4080

SUBJECT: ESTABLISHMENT EVALUATION REQUEST

NDA, ANDA, AND SUPPLEMENT NUMBER: 86-620 (10 mg), 86-621 (25 mg), 86-622 (50 mg)

DRUG TRADE MARK (if any) _____

DRUG NONPROPRIETARY NAME: Amitriptyline HCl Tablets

DOSAGE FORM AND STRENGTH(S): HCl

DRUG CLASSIFICATION: PROFILE CLASS CODE:
(Priority) _____ A or B _____ 1C _____ Other _____ _____

APPLICANT'S NAME: Danbury Pharmacal, Inc.
ADDRESS: 131 West Street, P.O. BOX 296, Danbury, CT 06810

FACILITIES TO BE EVALUATED: (Name, Full Address, DMF# (if any), and Responsibility)

1. applicant repackager USING

(b)4 - Confidential

approval of 86-610(10 mg)

86-859(25 mg)

86-857(50 mg)

Comments: ( ) See Attached. cc: DBarrow HFO-503 12-87
( ) Actual on-site inspection requested.

Reason: _____

****

FOR HFN-322 USE ONLY:

Request Rec'd: _____ Inspection Requested (if applicable) _____

Firm(s) are in Compliance With GMPs: _____
Basis for Decision: _____
Reviewing CSO: _____ Concurrance: _____

cc: HFN-____
HFN-____
HFN-322

FORM FDA 3274 (1/83)

JAN 5 1984

NDA 88-634

Danbury Pharmacal, Inc.
Attention: Nassim Maleh
131 West Street
P. O. Box 295
Danbury, CT 06810

Gentlemen:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NAME OF DRUG: Amitriptyline Hydrochloride Tablets, USP 100 mg

DATE OF APPLICATION: December 9, 1983

DATE OF RECEIPT: January 3, 1984

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the NDA number shown above.

Sincerely yours,

Marvin Seife 1/5/84

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs and Biologics

BOS-DO DUP HFN-530
JLMeyer/mlb/1-4-83
ack JLMeyer 1/4/84

NOTICE OF APPROVAL

NEW DRUG APPLICATION OR SUPPLEMENT

NDA NUMBER: 88-634

DATE APPROVAL LETTER ISSUED:

TO: Press Relations Staff (HFI-40)

FROM:
- [X] Bureau of Drugs
- [ ] Bureau of Veterinary Medicine

ATTENTION

Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.

TYPE OF APPLICATION
- [ ] ORIGINAL NDA
- [ ] SUPPLEMENT TO NDA
- [XX] ABBREVIATED ORIGINAL NDA
- [ ] SUPPLEMENT TO ANDA

CATEGORY
- [XX] HUMAN
- [ ] VETERINARY

TRADE NAME *(or other designated name)* AND ESTABLISHED OR NONPROPRIETARY NAME *(if any)* OF DRUG:

Amitriptyline Hydrochloride

DOSAGE FORM: Tablet ORIGINAL ABBREVIATED

HOW DISPENSED
- [X] RX
- [ ] OTC

ACTIVE INGREDIENT(S) *(as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)*

amitriptyline Hydrochloride, 100 mg.

NAME OF APPLICANT *(Include City and State)*

Danbury Pharmacal, Inc (Repackager)
Danbury, CT 06810

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY

Antidepressant

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

FORM PREPARED BY

NAME	DATE
C M Smith C M Smith	3-1-84

FORM APPROVED BY

NAME	DATE
J L Meyer	

FORM FD 1642 (2/75) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.